

JUN 03 2004

Express Mail No.:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: CAPON *et al.*

Confirmation No.: 9053

Application No.: 09/126,559

Group Art Unit: 1648

Filed: July 30, 1998

Examiner: Z. Lucas

For: COMPOSITIONS AND METHODS
FOR DETERMINING ANTI-VIRAL
DRUG SUSCEPTIBILITY AND
RESISTANCE AND ANTI-VIRAL
DRUG SCREENING

Attorney Docket No.: 011068-043-999

SECOND INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure provisions of 37 C.F.R. §1.56, there is hereby provided certain information which the Examiner may consider material to the examination of the subject U.S. patent application. It is requested that the Examiner make this information of record if it is deemed material to the examination of the application. This paper is being filed pursuant to C.F.R. § 1.34.

1. Enclosures accompanying this Information Disclosure Statement are:
 - 1a. A list of all patents, publications, applications, or other information submitted for consideration by the office.
 - 1b. A legible copy of :
 - Each U.S. patent application publication and U.S. and foreign patent;
 - Each publication or that portion which caused it to be listed on the PTO-1449;
 - For each cited pending U.S. application, the application specification including the claims, and any drawing of the application, or portion of the application which caused it to be listed on the PTO-1449 including any claims directed to that portion;
 - all other information or portion which caused it to be listed on the PTO-1449.
 - 1c. An English language copy of search report(s) from a counterpart foreign application or PCT International Search Report.
 - 1d. Explanations of relevancy (ATTACHMENT 1(d), hereto) or English language abstracts of the non-English language publications.
2. This Information Disclosure Statement is filed under 37 C.F.R. §1.97(b):
 - Within three months of the filing date of a national application other than a continued prosecution application under §1.53(d);

06/09/2004 05ANDARA 00000011 503013 09126559

01 FC:1806

100.00 DA

CAJD: 502875.1

- Within three months of the date of entry of the national stage as set forth in §1.491 in an international application;
 - Before the mailing of the first Office action on the merits;
 - Before the mailing of a first Office action after the filing of a request for continued examination under §1.114.
3. This Information Disclosure Statement is filed under 37 C.F.R. §1.97(c) after the period specified in 37 C.F.R. §1.97(b), but before the mailing date of any of a final action under 37 C.F.R. §1.113, a notice of allowance under 37 C.F.R. §1.311 or an action that otherwise closes prosecution in the application.

(Check either Item 3a or 3b)

- 3a. The Certification Statement in Item 5 below is applicable. Accordingly, no fee is required.
- 3b. The \$180.00 fee set forth in 37 C.F.R. §1.17(p) in accordance with 37 C.F.R. §1.97(c) is:
 enclosed
 to be charged to Jones Day Deposit Account No. 503013.

(Item 3b to be checked if any reference known for more than 3 months)

4. This Information Disclosure Statement is filed under 37 C.F.R. §1.97(d) after the period specified in 37 C.F.R. §1.97(c), but on or before the date of payment of the issue fee.

The \$180.00 fee set forth in 37 C.F.R. §1.17(p) is:

- enclosed.
 to be charged to Jones Day Deposit Account No. 503013.

The Certification Statement in Item 5 below is applicable.

5. Certification Statement (applicable if Item 3a or Item 4 is checked)

(Check either Item 5a or 5b)

- 5a. In accordance with 37 C.F.R. §1.97(e)(1), it is certified that each item of information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.
- 5b. Each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, and the communication was not **received** by any individual designated in 37 C.F.R. §1.56(c) more than thirty days prior to the filing of this information disclosure statement.
- 5c. Pursuant to 37 C.F.R. §1.704(d), each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, and the communication was not **received** by any individual designated in 37 C.F.R. §1.56(c) more than thirty days prior to the filing of this information disclosure statement.
6. This application is a continuation application under 37 C.F.R. §1.60 or §1.53(b) or (d).

(Check appropriate Items 6a, 6b and/or 6c)

- 6a. A Petition to Withdraw from issue under 37 C.F.R. §1.313(b)(5) is concurrently filed herewith.
- 6b. Copies of publications listed on Form PTO-1449 from prior, of which this application claims priority under 35 U.S.C. §120, are not being submitted pursuant to 37 C.F.R. §1.98(d).
- 6c. Copies of the publications listed on Form PTO-1449 were not previously cited in prior application, and are provided herewith.
7. This is a Supplemental Information Disclosure Statement. (Check Item 7a)
- 7a. This Supplemental Information Disclosure Statement under 37 C.F.R. §1.97(f) supplements the Information Disclosure Statement filed on . A bona fide attempt was made to comply with 37 C.F.R. §1.98, but inadvertent omissions were made. These omissions have been corrected herein. Accordingly, additional time is requested so that this Supplemental Information Disclosure Statement can be considered as if properly filed on
8. In accordance with 37 C.F.R. §1.98, a concise explanation of what is presently understood to be the relevance of each non-English language publication is:
- (Check Item 8a, 8b, or 8c)*
- 8a. satisfied because all non-English language publications were cited on the enclosed English language copy of the PCT International Search Report or the search report from a counterpart foreign application indicating the degree of relevance found by the foreign office.
- 8b. set forth in the application.
- 8c. enclosed as an attachment hereto.
9. The Commissioner is authorized to charge any additional fee required or credit any overpayment for this Information Disclosure Statement and/or Petition to Jones Day Deposit Account No. 503013.
10. No admission is made that the information cited in this Statement is, or is considered to be, material to patentability nor a representation that a search has been made (other than a search report of a foreign counterpart application or PCT International Search Report if submitted herewith). 37 C.F.R. §§1.97(g) and (h).

Respectfully submitted,

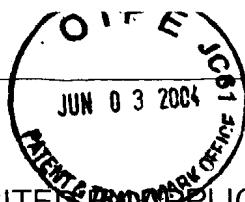


David Pauling for
Nikolaos C. George (Reg. No. 39,201)

P-56056
(Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 326-3939

Date: June 3, 2004



LIST OF REFERENCES CITED BY APPLICANT
(Use several sheets if necessary)

| | |
|----------------------------------|------------------------------|
| ATTY DOCKET NO. 11068-043-999 | APPLICATION NO 09/126,559 |
| APPLICANT Capon et al. | |
| FILING DATE July 30, 1998 | GROUP 1642 |

U.S. PATENT DOCUMENTS

| *EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLAS S | FILING DATE IF APPROPRIATE |
|-------------------|-----|-----------------|---------|------------------|-------|-----------|----------------------------|
| | A01 | 4,952,496 | 8/1990 | Studier et al. | | | |
| | A02 | 5,126,251 | 6/1992 | Moss et al. | | | |
| | A03 | 5,135,855 | 8/1992 | Moss et al. | | | |
| | A04 | 5,354,674 | 10/1994 | Hodgson | | | |
| | A05 | 5,462,873 | 10/1995 | Garfinkel et al. | | | |
| | A06 | 5,837,464 | 11/1998 | Capon et al. | | | |
| | A07 | 5,874,565 | 2/1999 | Rice et al. | | | |
| | A08 | 6,033,902 | 3/2000 | Haseltine et al. | | | |
| | A09 | 6,242,187 | 6/2001 | Capon et al. | | | |
| | A10 | 20020034732 | 3/2002 | Capon et al. | | | |

FOREIGN PATENT DOCUMENTS

| | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION | YES | NO |
|--|-----|---|---------|---------|-------|----------|-------------|-----|----|
| | A11 | WO91/19798 | 12/1991 | PCT | | | | | |
| | A12 | WO92/07943 | 5/1992 | PCT | | | | | |
| | A13 | WO94/19478 | 9/1994 | PCT | | | | | |
| | A14 | WO94/29438 | 12/1994 | PCT | | | | | |
| | A15 | WO95/22622 | 8/1995 | PCT | | | | | |
| | A16 | WO99/06597 | 2/1999 | PCT | | | | | |
| | A17 | International Search Report PCT/US97/01609 | 4/1997 | PCT | | | | | |
| | A18 | International Search Report PCT/US98/15967 | 10/1998 | PCT | | | | | |
| | A19 | International Search Report PCT/US2003/013791 | 4/2004 | PCT | | | | | |

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

| | |
|-----|---|
| A20 | Alam et al., "Reporter Genes: Application to the Study of Mammalian Gene Transcription," (1990), Analytical Biochemistry 188:245-254. |
| A21 | Bernard, "Positive Selection of Recombinant DNA by CcdB," (1996), Biotechniques 21:320-323. |
| A22 | Blight et al., "Efficient Initiation of HCV RNA Replication in Cell Culture," (2000), Science 290:1972-1974 |
| A23 | Chalfie, "Green Fluorescent Protein," (1995), Photochemistry and Photobiology, 62:651-656. |
| A24 | Cheng et al., "Specific Interaction Between the Hepatitis C Virus Ns5B RNA Polymerase and the 3' End of the Viral RNA," (1999), J. Virol. 73:7044-7049. |

| | |
|-----|--|
| A25 | Chowrira et al., "In Vitro and in Vivo Comparison of Hammerhead Hairpin, and Hepatitis Delta Virus Self Processing Ribozyme Cassettes," (1994), J. Biol. Chem. 269: 25856-25864. |
| A26 | Chung et al., "Hepatitis C Virus Replication is Directly Inhibited By IFN- α in a Full Length Binary Expression System," (2001), 98:9847-9852. |
| A27 | Frese et al., "Interferon- γ Inhibits Replication of Subgenomic and Genomic Hepatitis C Virus RNAs," (2002), Hepatology 35:694-703. |
| A28 | Gould et al., "Firefly Luciferase as a Tool in Molecular and Cell Biology," (1988), Analytical Biochemistry 175:5-13. |
| A29 | Grakoui et al., "Characterization of the Hepatitis C Virus-Encoded Serine Proteinase: Determination of Proteinase-Dependent Polyprotein Cleavage Sites," (1993), J. Virol. 67:2832-2843. |
| A30 | Guo et al., "Effect of Alpha Interferon on the Hepatitis C Virus Replicon," (2001) J. Virol. 75:8516-8523. |
| A31 | Hiramatsu et al., "HCV cDNA Transfection to HepG2 Cells," (1997), J. Viral Hepatol., 4(suppl.1):61-67. |
| A32 | Hoshida et al., "Improvement of Chemosensitivity Prediction by Transcriptional Profiling in Hepatoma Cells," (2001), Genome Informatics 12:257-58 |
| A33 | Ikeda et al., "Selectable Subgenomic and Genome-Length Dicistronic RNAs Derived from an Infectious Molecular Clone of the HCV-N Strain of Hepatitis C Virus Replicate Efficiently in Cultured Huh7 Cells" (2002) J. Virol. 76:2997-3006. |
| A34 | Kawai et al., " α -Fetoprotein-Producing Hepatoma Cell Lines Share Common Expression Profiles of Genes in Various Categories Demonstrated by cDNA Microarray Analysis" (2001), Hepatology 33:676-691. |
| A35 | Krieger et al., "Enhancement of Hepatitis C Virus RNA Replication by Cell Culture-Adaptive Mutations," (2001), J Virol 75:4614-24. |
| A36 | Lohmann et al., "Replication of Subgenomic Hepatitis C Virus RNAs in a Hepatoma Cell Line" (1999), Science, 285:110-113. |
| A37 | Lohmann et al., "Mutations in Hepatitis C Virus RNAs Conferring Cell Culture Adaptation," (2001), J. Virol. 75:1437-1449. |
| A38 | Mizutani et al., "Characterization of Hepatitis C Virus Replication in Cloned Cells Obtained from a Human T-Cell Leukemia Virus Type 1-Infected Cell Line, MT-2," (1996), J. Virol. 70:7219-7223 |
| A39 | Moore et al., "The Development of β -Lactamase as a Highly Versatile Genetic Reporter for Eukaryotic Cells," (1997) Analytical Chemistry 247:203-209. |
| A40 | Mulligan et al., "Expression of a Bacterial Gene In Mammalian Cells," (1980), Science 209: 1422-1427. |
| A41 | Olesen et al., "Detection of β -Glactosidase and β -Glucuronidase Using Chemiluminescent Reporter Gene Assays," Methods in Molecular Biology, Recombinant Protein Protocols: Detection and Isolation, 63:61-70. |
| A42 | Perotta et al., "A Pseudoknot-Like Structure Required for Efficient Self-Cleavage of Hepatitis Delta Virus RNA," (1991), Nature 350:434-436. |
| A43 | Pflugheber et al., "Regulation of PKR and IRF-1 During Hepatitis C Virus RNA Replication," (2002), PNAS 99: 4650-4655. |
| A44 | Pietsch, et al., "Characterization of the Continuous Cell Line HepT1 Derived from a Human Hepatoblastoma," (1996), Lab Invest 74:809-818. |
| A45 | Pietschmann et al., "Persistent and Transient Replication of Full Length Hepatitis C Virus Genomes in Cell Culture," (2002), J. Virol. 76:4008-4021. |
| A46 | Schenborn et al., "Reporter Gene Vectors and Assays," (1999), Molecular Biotechnology 13:29-44. |
| A47 | Shimizu et al., "Neutralizing Antibodies Against Hepatitis C Virus and the Emergence of Neutralization Escape Mutant Viruses," (1994), J. Virol. 68:1494-1500. |
| A48 | Shimizu et al., "Multicycle Infection of Hepatitis C Virus in Cell Culture and Inhibition by Alpha and Beta Interferons," (1994), J. Virol. 68:8406-8408. |
| A49 | Shimizu et al., "Correlation Between the Infectivity of Hepatitis C Virus <i>In Vivo</i> and its Infectivity <i>In Vitro</i> ," (1993), PNAS 90:6037-6041. |
| A50 | Shimizu et al., "Evidence for <i>In Vitro</i> Replication of Hepatitis C Virus Genome in a Human T-Cell Line," (1992) , PNAS 89:5477-5481. |

JUN 03 2004

A51

Southern et al., "Transformation of Mammalian Cells to Antibiotic Resistance with a Bacterial Gene Under Control of the SV40 Early Region Promoter," (1982), J. Molec. Appl. Genet. 1:327-341.

A52

Steinkühler et al., "Activity of Purified Hepatitis C Virus Protease NS3 on Peptide Substrates," (1996), J. Virol. 70:6694-6700.

A53

Sugden et al., "A Vector that Replicates as a Plasmid and can be Efficiently Selected in B-Lymphoblasts Transformed by Epstein-Barr Virus," (1985), Mol. Cell. Biol. 5, 410-413.

A54

Valli et al., "Hepatitis C Virus Infection of a Vero Cell Clone Displaying Efficient Virus-Cell Binidng," (1997), Res. Virol. 148:181-186.

A55

Vassilev et al., "Authentic and Chimeric Full-Length Genomic cDNA Clones of Bovine Viral Diarrhea Virus That Yield Infectious Transcripts," (1997), J. Virol. 71:471-478

A56

Wadkins et al., "Ribozyme Activity in the Genomic and Antigenomic RNA Strands of Hepatitis Delta Virus," (2002), Cell Mol. Life Sci. 59:112-25.

A57

Witherell et al., "Statistical Analysis of Combined Substitutions in Nonstructural 5A Region of Hepatitis C Virus and Interferon Responses," (2001), J. Med. Virol. 63:8-16.

A58

Wright-Minogue et al., "Cross-Genotypic Interaction Between Hepatitis C Virus NS3 Protease Domains and NS4A Cofactors," (2000), J. Hepatology 32:497-504.

A59

Yang et al., "Quantification of Gene Expression with a Secreted Alkaline Phosphatase Reporter System," (1997), BioTechniques 23:1110-1114.

A60

Yoo et al., "Transfection of a Differentiated Human Hepatoma Cell Line (Huh7) with In Vitro Transcribed Hepatitis C Virus (HCV) RNA and Establishment of a Long-Term Culture Persistently Infected With HCV," (1995), 69:32-38.

A61

Zlokarnik, "Fusions to β -Lactamase as a Reporter for Gene Expression in Live Mammalian Cells," (2000), Methods in Enzymology 326:221-241.

A62

Danos, Olivier and Mulligan, Richard C. "Safe and Efficient Generation of Recombinant Retroviruses with Amphotropic and Ecotropic Host Ranges" Proc. Natl. Acad. Sci. USA (Sep. 1988) vol. 85, pp. 6460-6464.

A63

Fuerst, Thomas R., and Moss, Bernard "Structure and Stability of mRNA Synthesized by Vaccinia Virus-encoded Bacteriophage 17 RNA Polymerase in Mammalian Cells" J. Mol. Biol. (1989) vol. 206, pp. 333-348.

A64

Lieber, Andre, et al., "High Level Gene Expression in Mammalian Cells by a Nuclear 17-Phage RNAPolymerase" Nucleic Acids Research (1989) vol. 17, No. 21, pp. 8485-8493.

A65

Larder, Brendan A., et al., "HIV with Reduced Sensitivity to Zidovudine (AZT) Isolated During Prolonged Therapy" Science (Mar. 31, 1989) vol. 243, pp.1731-1734.

A66

Andreasson, K.I., et al., "Production of Pro-Opiomelanocortin (POMC) by a Vaccinia Virus Transient Expression System and In Vitro Processing of the Expressed Prohormone by POMC-converting Enzyme" FE.B.S Letters (May 1989) vol. 248, No. 1.2 pp. 43-47.

A67

Elroy-Stein, Orna, et al., "Cap-Independent Translation of mRNA Conferred by Encephalomyocarditis Virus 5' Sequence Improves the Performance of the Vaccinia Virus/Bacteriophage T7 Hybrid Expression System" Proc. Natl. Acad. Sci. USA (Aug. 1989) vol. 86, pp. 6126-6130.

A68

Larder, Brendan A., and Sharon D.Kemp, "Multiple Mutations in HIV-1 Reverse Transcriptase confer High-Level Resistance of Zidovudine (AZT)" Science (Dec. 1089) vol. 246, pp. 1155-1158.

A69

Elroy-Stein, Orna and Bernard Moss, "Cytoplasmic Expression System Based on Constructive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells" Proc. Natl. Acad. Sci. USA (Spe. 1990) vol. 87, pp. 6743-6747.

A70

Page, Kathleen A., et al., "Construction and Use of a Human Immunodeficiency Virus Vector for Analysis of Virus Infectivity" Journal of Virology (Nov. 1990) vol. 64, No. 11, pp. 5270-5276.

A71

Moss, B et al., "New Mammalian Expression Vectors" Nature (Nov. 1990) vol. 348, pp. 91-92.

A72

Deng, Hong, et al., "High-Efficiency Protein Synthesis from T7 RNA Polymerase Transcripts in 3T3 Fibroblasts" GENE (1991)pp. 193-201.

A73

Goldman, Mark E., et al., "L-696,229 Specifically Inhibits Human Immunodeficiency Virus Type 1 Reverse Transcriptase and Possesses Antiviral Activity In Vitro" Antimicrobial Agents and Chemotherapy (May 1992) vol. 36, No. 5, pp. 1019-1023.

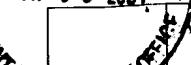
JUN 03 2004 C-1

| | |
|-----|---|
| A74 | Saari, Walfred, S., et al. "2-Pyridinone Derivatives: A New Class of Nonnucleoside HIV-1 Spedivid Reverse Transcriptase Inhibitors" Journal of Medicinal Chemistry (1991) vol. 34, No. 9, pp. 2922-2925. |
| A75 | Landau, Nathaniel, R., et al., "Pseudotyping with Human T-Cell Leukemia Virus Type I Broadens the Human Immunodeficiency Virus Host Range" Journal of Medicinal Chemistry (1991) vol. 34, No. 9, pp 2922-2925. |
| A76 | Goldman, Mark E., et al., "Pyridinone Derivatives: Specific Human Immunodeficiency Virus Type 1 Reverse Transcriptase Inhibitors with Antiviral Activity" Proc. Natl. Acad. Sci. USA (Aug. 1991) vol. 88, pp. 6863-6867. |
| A77 | Nunberg, Jack H., et al., "Viral Resistance to Human Immunodeficiency Virus Type-1 Specific Pyridinone Reverse Transcriptase Inhibitors" Journal of Virology (Sep. 1991) vol. 65, No. 9, pp. 4887-4892. |
| A78 | St. Clair, M.H., et al. "Resistance to ddl and Sensitivity to AZT Induced by a Mutation in HIV-1 Reverse transcriptase" Science (Sep. 27, 1991) vol. 253, pp. 1557-1559. |
| A79 | Huang, Mingjun and Summers, Jesse "Infection Initiated by the RNA Pregenome of a DNA Virus" Journal of Virology (Oct. 1991) vol. 65, No. 10, pp. 5435-543. |
| A80 | Larder, Brendan, A., et al., "Zidovudine-Resistant Human Immunodeficiency Virus Selected by Passage in Cell Culture" Journal of Virology (Oct. 1991) vol. 65, No. 10, pp. 5232-5236. |
| A81 | Homberger, F.R., et al. "Detection of Rodent Coronaviruses in Tissues and Cell Cultures by Using Polymerase Chain Reaction" J. Clin. Microbiol (Dec. 1991) vol. 29:2789-2793. |
| A82 | Sardana, Vinod, V, et al., "Functional Analysis of HIV-1 Reverse Transcriptase Amino Acids Involved in Resistance to Multiple Nonnucleoside Inhibitors" Journal of Biological Chemistry (1992) vol. 267, No. 25, pp. 17526-17530. |
| A83 | Yang, Xian-Cbeng, et al., "Cell-Specific Posttranslational Events Affect Functional Expression at the Plasma Membrane but not Tetrodotoxin Sensitivity of the Rat Brain VIA Sodium Channel a-Subunit Expressed in Mammalian Cells" The Journal of Neuroscience (Jan. 1992) vol. 12(1), pp. 268-277. |
| A84 | Richman, Douglas D. "Antiretroviral Drug Resistance: Mechanisms, Pathogenesis, Clinical Significance" pp. 1-13. |
| A85 | Condra, Jon H., et al., "Identification of the Human Immunodeficiency Virus Reverse Transcriptase Residues That Contribute to the Activity of Diverse Nonnucleoside Inhibitors" Antimicrobial Agents and Chemotherapy (Jul. 1992) vol. 36, No. 7, pp. 1441-1446. |
| A86 | Trono, Didier, "Partial Reverse Transcripts in Virions from Human Immunodeficiency and Murine Leukemia Viruses" Journal of Virology(Aug. 1992) vol. 66, No. 8, pp. 4893-4900. |
| A87 | Lori, Franco, et al., "Viral DNA Carried by Human Immunodeficiency Virus Type 1 Virions" Journal of Virology (Aug. 1992) vol. 66, No. 8, pp. 5067-5074. |
| A88 | Larder, Brendan A., "3' Azido-3'-Deoxythymidine Resistance Suppressed by a Mutation Conferring Human Immunodeficiency Virus Type 1 Resistance to Nonnucleoside Reverse Transcriptase Inhibitors" Antimicrobial Agents and Chemotherapy (Dec. 1992) vol. 36, No. 12, pp. 2664-2669. |
| A89 | Gu, Zhengxian, et al., "Novel Mutation in the Human Immunodeficiency Virus Type 1 Reverse Transcriptase Gene That Encodes Cross-Resistance to 2',3'-Dideoxyinosine and 2',3'-Dideoxycytidine" Journal of Virology (Dec. 1992) vol. 66, No. 12, pp. 7128-7135. |
| A90 | Baltimore, David, "The Treasure Under the Right Stone" Reverse Transcriptase (1993) pp. 1-3 |
| A91 | Larder, Brendan A., "Inhibitors of HIV Reverse Transcriptase as Antiviral Agents and Drug Resistance" Chapter 11 Reverse Transcriptase pp. 205-222 Cold Spring Harbor Laboratory Press (1993). |
| A92 | Gao, Xiang, and Huang, Leaf, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes" Nucleic acids Research (1993) vol. 21, No. 12, pp. 267-2872. |
| A93 | Gottesman, Michael M., and Pastan, Ira, "Biochemistry of Multidrug Resistance Mediated by the Multidrug Transporter" Annu. Rev. Biochem. (1993) vol. 62, pp. 385-427 |
| A94 | Le Grice, Stuart F.J., "Human Immunodeficiency Virus Reverse Transcriptase" Reverse Transcriptace (1993) pp. 163-191. |
| A95 | Telesnitsky, Alice and Goff, Stephen P., "Strong-stop Strand transfer during Reverse Transcription" Reverse Transcriptase (1993) pp. 49-83. |

JUN 03 2006

| | |
|------|---|
| A96 | Wlodawer, Alexander and Erickson, John W., "Structure Based Inhibitors of HIV-1 1 Protease" Annu. Rev. Biochem. (1993) vol. 62, pp. 543-585. |
| A97 | Richman, Douglas D., "HIV Drug Resistance" Annu. Rev. Pharmacol. Toxicol. (1993) vol. 32, pp. 149-164. |
| A98 | Sandig, Volker, et al., "A Phage T7 Class-III Promoter Functions as a Polymerase II Promoter in Mammalian Cells" GENE (1993) pp. 255-259. |
| A99 | Lieber, Andre, et al., "A Mutant T7 Phage Promoter is Specifically Transcribed by T7-RNA Polymerase in Mammalian Cells" Eur. J. Biochem. (1993) vol. 217, pp. 387-394. |
| A100 | Chattopadhyay, Sisir K., et al., "Genomes of Murine Leukemia Viruses Isolated from Wild Mice" Journal of Virology (Sep. 1981) vol. 39, No. 3, pp. 777-791. |
| A101 | Richman, Douglas D., "Minireview, Resistance of Clinical Isolates of Human Immunodeficiency Virus to Antiretroviral Agents" Antimicrobial Agents and Chemotherapy (June 1993) vol. 37, No. 6, pp. 1207-1213. |
| A102 | Richardson, Jennifer H., et al., "Packaging of Human Immunodeficiency Virus Type 1 RNA Requires cis-Acting Sequences Outside the 5' Leader Region" Journal of Virology (July 1993) vol. 67, No. 7, pp. 3997-4005. |
| A103 | Byrnes, Vera W., et al., "Comprehensive Mutant Enzyme and Viral Variant Assessment of Human Immunodeficiency Virus Type 1 Reverse Transcriptase Resistance to Nonnucleoside Inhibitors" Antimicrobial Agents and Chemotherapy (Aug. 1993) vol. 37, No. 8, pp. 1576-1579. |
| A104 | Emini, Emilio A., et al., "HIV-1 Error Revealed" Nature (Aug. 19, 1993) vol. 364, pp. 679. |
| A105 | Balzarini, Jan et al., "Treatment of Human Immunodeficiency Virus Type 1 (HIV-1)-Infected Cells with Combinations of HIV-1-Specific Inhibitors Results in a Different Resistance Pattern Than Does Treatment with Single-Drug Therapy" Journal of Virology (Sep. 1993) vol. 67, No. 9, pp. 5353-5359. |
| A106 | Larder, Brendan A., et al., "Convergent Combination Therapy can Select Viable Multidrug-Resistant HIV-1 In Vitro" Nature (Sep. 30, 1993) vol. 365, pp. 451-453. |
| A107 | Sag, Michael S., et al., "A short Term Clinical Evaluation of L-697,661, A Non-Nucleoside Inhibitor of HIV-1 Reverse Transcriptase" The New England Journal of Medicine (Oct. 7, 1993) vol. 329, No. 15, pp. 1065-1072. |
| A108 | Boyer, Paul L. et al., "Mutational Analysis of the Fingers and Palm Subdomains of Human Immunodeficiency Virus Type-1 (HIV-1) Reverse Transcriptase" J. Mol. Biology (1994) vol. 243, pp. 472-483. |
| A109 | Deng, Hong, and Wolff, Jon A., "Self-Amplifying Expression from the 17 Promoter in 3D Mouse Fibroblasts" GENE (1994) pp. 245-249. |
| A110 | Richman, Douglas D., "Resistance, Drug Failure, and Disease Progression" AIDS research and Human Retroviruses (1994) vol. 10, No. 8, pp. 901-905. |
| A111 | Ansari-Lari, M. Ali and Gibbs, Richard A., "Analysis of HIV Type 1 Reverse Transcriptase Expression in a Human Cell Line" AIDS Research and Human Retroviruses (1994) vol. 10, No. 9, pp. 1117-1124. |
| A112 | Mirochnitchenko, Oleg, et al., "Production of Single-Stranded DNA in Mammalian Cells by Means of a Bacterial Retron" The Journal of Biological Chemistry (Jan. 1994) vol. 269, No. 4, pp. 2380-2383. |
| A113 | Katz, Richard A., and Skalka, Anna Marie "The Retroviral Enzymes" Annu. Rev. Biochem. (1994) vol. 63, pp. 133-173. |
| A114 | Chen, Xiaozhuo, et al., "A Self-Initiating Eukaryotic Transient Gene Expression System Based on Cotransfection of Bacteriophage T7 RNA Polymerase and DNA Vectors Containing a T7 Autogene" NucleicAcids Research (1994) vol. 22, No. 11, pp. 2114-2120. |
| A115 | Kellam, Paul, et al., "Zidovudine Treatment Results in the Selection of Human Immunodeficiency Virus Type 1 Variants Whose Genotypes Confer Increasing Levels of Drug Resistance" Journal of General Virology (1994) vol. 75, pp. 341-351. |
| A116 | Kellam, Paul, and Larder, Brendan A., "Recombinant Virus Assay: a Rapid, Phenotypic Assay for Assessment of Drug Susceptibility of Human Immunodeficiency Virus Type 1 Isolates" Antimicrobial Agents and Chemotherapy (1994) vol. 38, No. 1, pp. 23-30. |
| A117 | El-Farrash, Mohamed A., et al., "Generation and Characterization of a Human Immunodeficiency Virus Type 1 (HIV-1) Mutant Resistant to an HIV-1 Protease Inhibitor" Journal of Virology (Jan. 1994) vol. 68, No. 1, pp. 233-239. |

JUN 03 2004



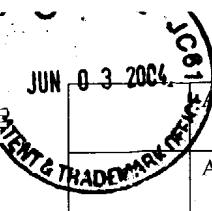
| | |
|------|--|
| A118 | Chen, Benjamin K., et al., "Distinct Modes of Human Immunodeficiency Virus Type 1 Retroviral Latency Revealed by Superinfection of Nonproductively Infected Cell Lines with Recombinant Luciferase Encoded Viruses" Journal of Virology (Feb. 1994) vol. 68, No. 2, pp. 654-660. |
| A119 | Richman, Douglas D., et al., "Nevirapine Resistance Mutations of Human Immunodeficiency Virus Type 1 Selected During Therapy" Journal of Virology (Mar. 1994) vol. 68, pp. 1660-1666. |
| A120 | Ho, David D., et al., "Characterization of Human Immunodeficiency Virus Type 1 Variants with Increased Resistance to a C ₂ -Symmetric Protease Inhibitor" Journal of Virology (Mar. 1994) vol. 68, No. 3, pp. 2016-2020. |
| A121 | Boyer, Paul L. et al., "Sensitivity of Wild-Type Human Immunodeficiency Virus Type 1 Reverse Transcriptase to Dideoxynucleotides Depends on Template Length; The Sensitivity of Drug-Resistant Mutants Does Not" PNAS (May 1994) vol. 91, pp. 4882-4886. |
| A122 | Brynes, Vera W., et al. "Susceptibilities of Human Immunodeficiency Virus Type 1 Enzyme and Viral Variants Expressing Multiple Resistance-Engendering Amino Acid Substitutions to Reverse Transcriptase Inhibitors" Antimicrobial Agents and Chemotherapy (Jun. 1994) vol. 38, No. 6, pp. 1404-1407. |
| A123 | Parolin, Cristina, et al., "Analysis in Human Immunodeficiency Virus Type 1 Vectors of cis-Acting Sequences That Affect Gene Transfer into Human Lymphocytes" Journal of Virology (Jun. 1994) vol. 68, No. 6, pp. 3888-3895. |
| A124 | Carroll, Richard, et al., "A Human Immunodeficiency Virus Type 1(HIV-1)-Based Retroviral Vectorty System Utilizing Stable HIV-1 Packaging Cell Lines" Journal of Virology (Sep. 1994) vol. 68, No. 9, pp. 6047-6051. |
| A125 | Richman, Douglas D., "Drug Resistance in Viruses" Trends in Microbiology (Oct. 10, 1994) vol. 2, No. 10, pp. 401-408. |
| A126 | Zhang, Hui, et al., "Intravirion Reverse Transcripts in the Peripheral Blood Plasma of Human Immunodeficiency Virus Type 1-Infected Individuals" Journal of Virology (Nov. 1994) vol. 68, No. 11, pp. 7591-7597. |
| A127 | Kalderon, Daniel, et al., "A Short Amino Acid Sequence Able to Specify Nuclear Location" Cell (Dec. 1984 - Part 2) vol. 39, pp. 499-509. |
| A128 | Ho, David D. "Time to Hit HIV, Early and Hard" The New England Journal of Medicine (1995) vol. 333, No. 7, pp. 450-451. |
| A129 | Wyatt, Linda S., et al., "Replication-Deficient Vaccinia Virus Encoding Bacteriophage T7 RNA Polymerase for Transient Gene Expression in Mammalian Cells" Virology (1995) vol. 210, pp. 202-205. |
| A130 | Ward, George A., et al., "Stringent Chemical and Thermal Regulation of Recombinant Gene Expression by Vaccinia Virus Vectors in Mammalian Cells" Proc. Natl. Acad. Sci. USA (1995) pp. 6773-6777. |
| A131 | Wei, Xiping, et al., "Viral Dynamics in Human Immunodeficiency Virus Type 1 Infection" Nature Pan. 1995) vol. 373, pp. 117-122. |
| A132 | Richman, Douglas D., "Drug Resistance in Relation to Pathogenesis" AIDS (1995) vol. 9 (Suppl A) pp. S49-S53. |
| A133 | Volberding, Paul, "The Need for Additional Options in the Treatment of Human Immunodeficiency Virus Infection" The Journal of Infectious Diseases (1995) vol. 17 (Suppl 2) pp. S150-S154. |
| A134 | Coffin, John M. "HIV Population Dynamics in Vivo: Implications for Genetic Variation, Pathogenesis, and Therapy" Science (Jan. 27, 1995) vol. 267, pp. 483-489. |
| A135 | Kim Baek and Loeb Lawrence, A "Human Immunodeficiency Virus Reverse Transcriptase Substitutes for DNA Polymerase in <i>Escherichia Coli</i> " P.N.A.S. I vol. 92, pp. 684-688. |
| A136 | Wain-Hobson, Simon "Virological Mayhem" Nature (Jan. 1995) vol. 373, p. 102. |
| A137 | Ho, David D., et al., "Rapid Turnover of Plasma Virions and CD4 Lymphocytes in HIV-1 Infection" Nature (Jan. 1995) pp. 123-126. |
| A138 | D'Aquila, Richard T., et al., "Zidovudine Resistance and HIV-1 Disease Progression During Antiretroviral Therapy" Annals of Internal Medicine (Mar. 15, 1995) vol. 122, No. 6, pp. 401-408. |
| A139 | Condra, John H., et al., "In Vivo Emergence of HIV-1 Variants Resistant to Multiple Protease Inhibitors" Nature (Apr. 6, 1995) vol. 374, pp. 569-571. |

JUN 03 2004



| | |
|------|--|
| A140 | Boyer, Paul L., and Hughes, Stephen H., "Analysis of Mutations at Position 184 in Reverse Transcriptase of Human Immunodeficiency Virus Type 1" <i>Antimicrobial Agents and Chemotherapy</i> (Jul. 1995) vol. 39, No. 7, pp. 1624-1628. |
| A141 | He, Jianglin, and Landau, Nathaniel R., "Use of a Novel Human Immunodeficiency Virus Type 1 Reporter Virus Expressing Human Placental Alkaline Phosphatase To Detect an Alternative Viral Receptor" <i>Journal of Virology</i> (Jul. 1995) vol. 69, No. 7, pp. 4587-4592. |
| A142 | Kim, Baek and Loeb, Lawrence A, "A Screen in Escherichia coli for Nucleoside Analogs That Target Human Immunodeficiency Virus (HIV) Reverse Transcriptase: Coexpression of HIV Reverse Transcriptase and Herpes Simplex Virus Thymidine Kinase" <i>Journal of Virology</i> (Oct. 1995) vol. 69, No. 10, pp. 6563-6566. |
| A143 | Saunders, J., and Cameron, J.M., "Recent Development in the Design of Antiviral Agents" <i>Med Res. Rev.</i> (Nov. 1995) vol. 15:497-531. |
| A144 | Young, Steven D., et al., "L-743,726 (DMP-266): a Novel, Highly Potent Nonnucleoside Inhibitor of the Human Immunodeficiency Virus Type 1 Reverse Transcriptase" <i>Antimicrobial Agents and Chemotherapy</i> (Dec. 1995) vol. 39, No. 12, pp. 2602-2605. |
| A145 | Goldman, Mark E., et al., "A Nonnucleoside Reverse Transcriptase Inhibitor Active on Human Immunodeficiency Virus Type 1 Isolates Resistant to Related Inhibitors!" <i>Antimicrobial Agents and Chemotherapy</i> (May 1993) vol 37, No. 5, pp. 947-949. |
| A146 | Fang, Guowei, et al., "Molecular Cloning of Full-Length HIV-1 Genomes Directly from Plasma Viral RNA" <i>Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology</i> (1996) vol. 12, No. 4, pp. 352-357. |
| A147 | Heid, Christian A., et al., "Real Time Quantitative PCR" <i>Genome Research</i> (1996) pp. 986-994. |
| A148 | Romeyn, Mary, "Report from the 3rd Conference of Retroviruses and Opportunistic Infections" <i>BETA</i> (Mar. 1996). |
| A149 | Schapiro, Jonathan, M., "Causes of Long Term Efficacy and/or Drug Failure in Protease (PR) Inhibitor Monotherapy" <i>ICA Abstracts</i> . |
| A150 | Mamatora, Gargi, et al., "HIV-1 Genechip™ and Dideoxynucleotide Sequence Analysis of HIV-1 Genomes Present in Plasma Samples from Patients of ACTG 143 Study" <i>ICA Abstracts</i> . |
| A151 | Garrett, Miyada, C., et al., "Sequencing HIV Isolates Using the Genechip™ HIV PRT Assay" <i>ICA Abstracts</i> . |
| A152 | Gingeras, Thomas R., et al. "Detection of Rifampin Conferring Mutations and Mycobacteria Speciation Using Myco Genechip™" <i>ICA Abstracts</i> . |
| A153 | Fischl, Margaret A., "Treatment of HIV Infection" Section II-Management of HIV Infections and Their Complications, Chapter 8, pp. 141-160. |
| A154 | Saag, Michael S. "AIDS Testing Now and in the Future" Section I-The Virus: Its Transmission and Infection, Chapter 4, pp. 65-88, 1994. |
| A155 | Richman, Douglas, D., "Antiviral Drug Resistance: Issues and Challenges" <i>Antiviral Drug Resistance</i> , Introductory Chapter, pp. 1-19. |
| A156 | Japour, Anthony J., "Standardized Peripheral Blood Mononuclear Cell Culture Assay for Determination of Drug Susceptibilities of Clinical Human Immunodeficiency Virus Type 1 isolates" <i>Antimicrobial Agents and Chemotherapy</i> (May 1993) vol. 37, pp. 1095-1101. |
| A157 | Pauwels, Rudi, et al. "Rapid and Automated Tetrazoliumbased Colorimetric Assay for the Detection of anti-HIV Compounds" <i>Journal of Virological Methods</i> (1988) vol. 20, pp. 309-321. |
| A158 | Larder, B. A., (1994) "Interactions Between Drug Resistance Mutations In Human Immunodeficiency Virus Type 1 Reverse Transcriptase" <i>Journal of General Virology</i> , 75:951-957. |
| A159 | Piatak, Jr., M., et al. (1993) "High Levels of HIV-1 In Plasma During All Stages Of Infection Determined By Competitive PCR" <i>Science</i> 259:1749-1754. |
| A160 | Popovic, M., et al. (1984) "Detection, Isolation, and Continuous Production Of Cytopathic Retroviruses (HTLV-III) From Patients With AIDS And Pre-AIDS" <i>Science</i> , 224:497-500. |
| A161 | Saltarelli, M. J., et al. (1993) "The CAEV tat Gene Transactivates The Viral LTR And Is Necessary For Efficient Viral Replication" <i>Virology</i> , 197:35-44. |
| A162 | Urdea, M. S., (1993) "Synthesis And Characterization of Branched DNA (bDNA) For The Direct And Quantitative Detection Of CMV, HBV, HCV, and HIV" <i>Clin. Chem.</i> 39:725-726. |

JUN 03 2004



| | |
|------|--|
| A163 | Allain, J., et al. (1987) "Long-Term Evaluation Of HIV Antigen And Antibodies To p24 And gp41 In Patients With Hemophilia" N. EngL J. Med., 317:1114-1121. |
| A164 | Barre-Sinoussi, F. et al. (1983) "Isolation Of A T-Lymphotropic Retrovirus From A Patient At Risk For Acquired Immune Deficiency Syndrome (AIDS)" Science 220:868-871. |
| A165 | Geodert, J. J., et al. (1987) "Effect Of T4 Count And Cofactors On The Incidence Of AIDS In Homosexual Men Infected With Human Immunodeficiency Virus", Jama 257:331-334. |
| A166 | Database Medline, US Nat. Lib., No. 97151131, Filocamo, G. et al. "Chimeric Sindbis Viruses dependent on NS3 protease of hepatitis C virus" J of Virology, (1997) 71(2):1117-27. |

EXAMINER**DATE CONSIDERED**

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with **MPEP 609**; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.